

Stability of Enkephalin and Cetyl-PEG₂-Enkephalin in Rat Brain Homogenate

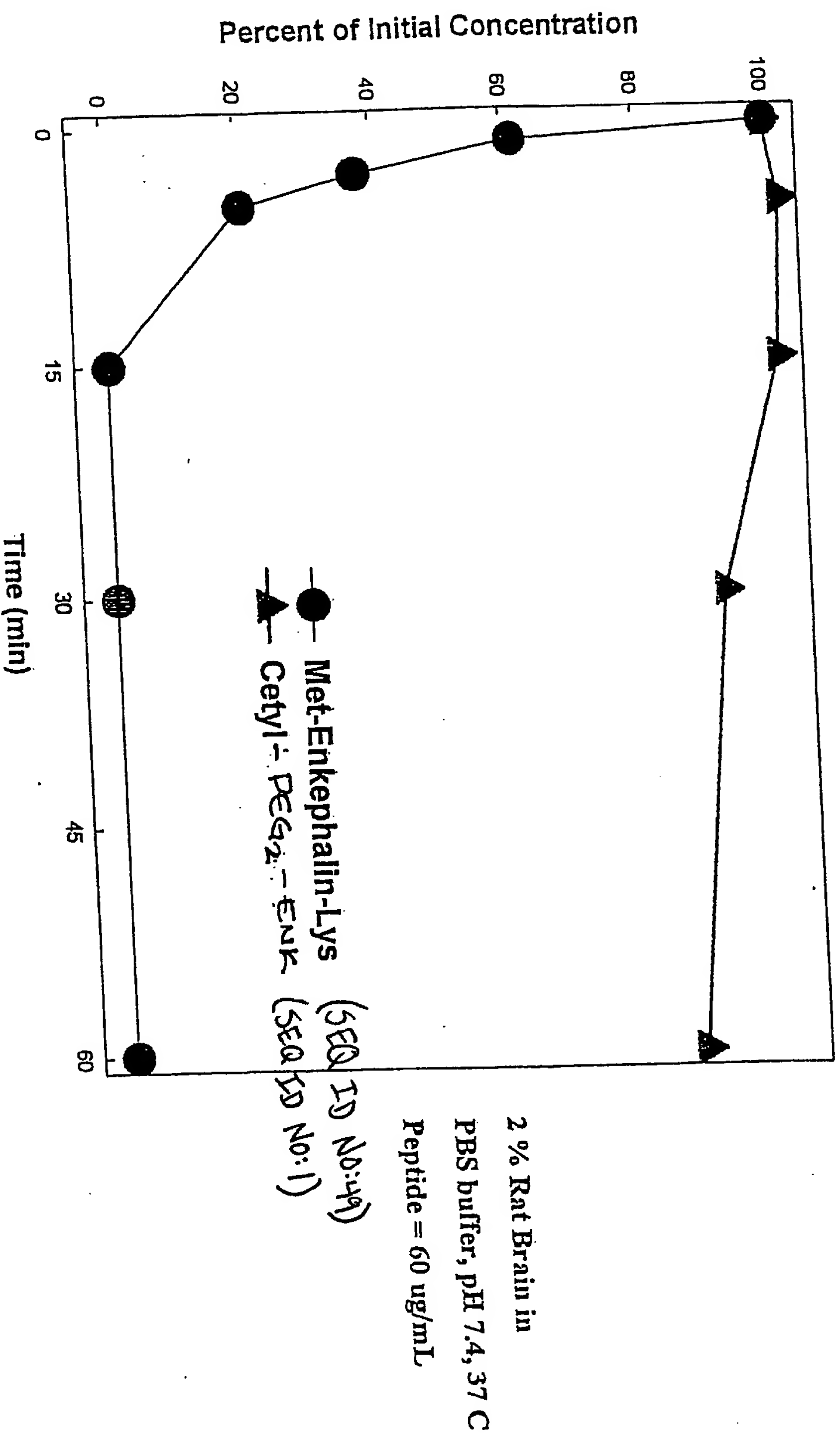


FIGURE 2

Stability of Cetyl-PEG₂ Enkephalin in Rat Brain Homogenate

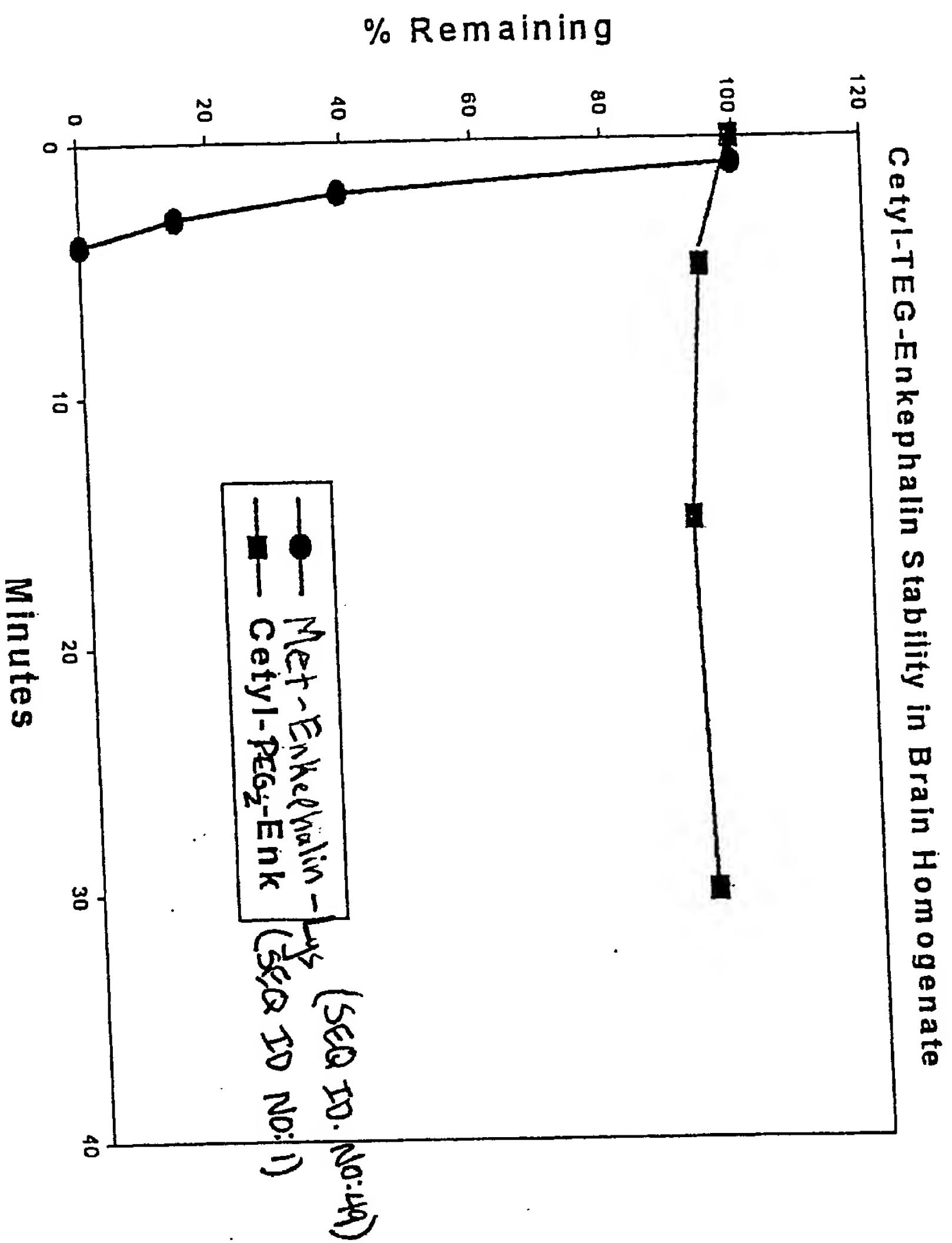


FIGURE 3

2 % w/v Rat brain in
PBS buffer, pH 7.4, 37 C
Peptide = 60 ug/mL

Stability of Palmitate-Peg₃-Enkephalin in Rat Brain Homogenate

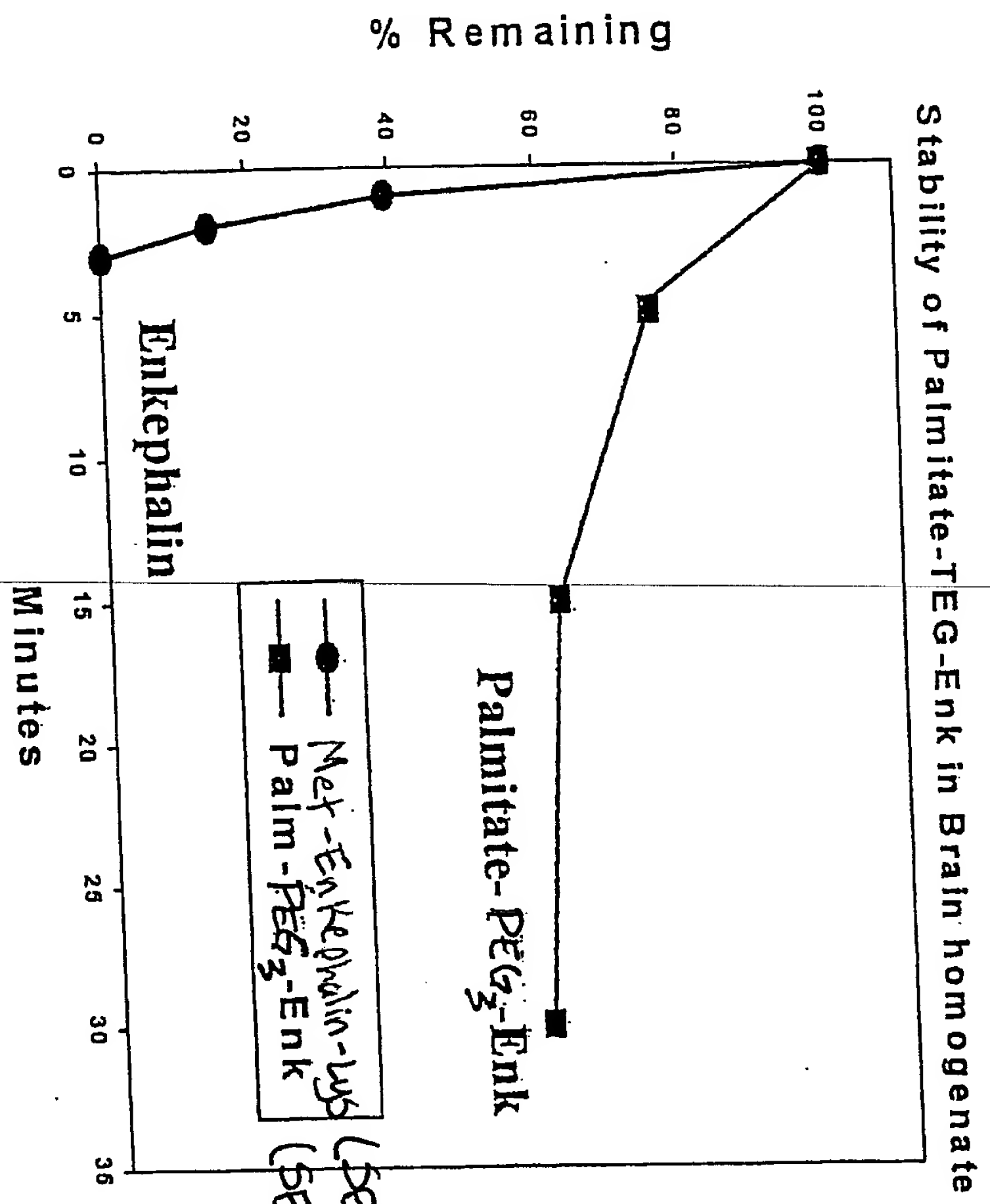


FIGURE 4.

2% w/v Rat Brain in
PBS buffer, pH 7.4, 37 C
Peptide = 60ug/mL

(SEQ ID NO:49)
(SEQ ID NO:1)

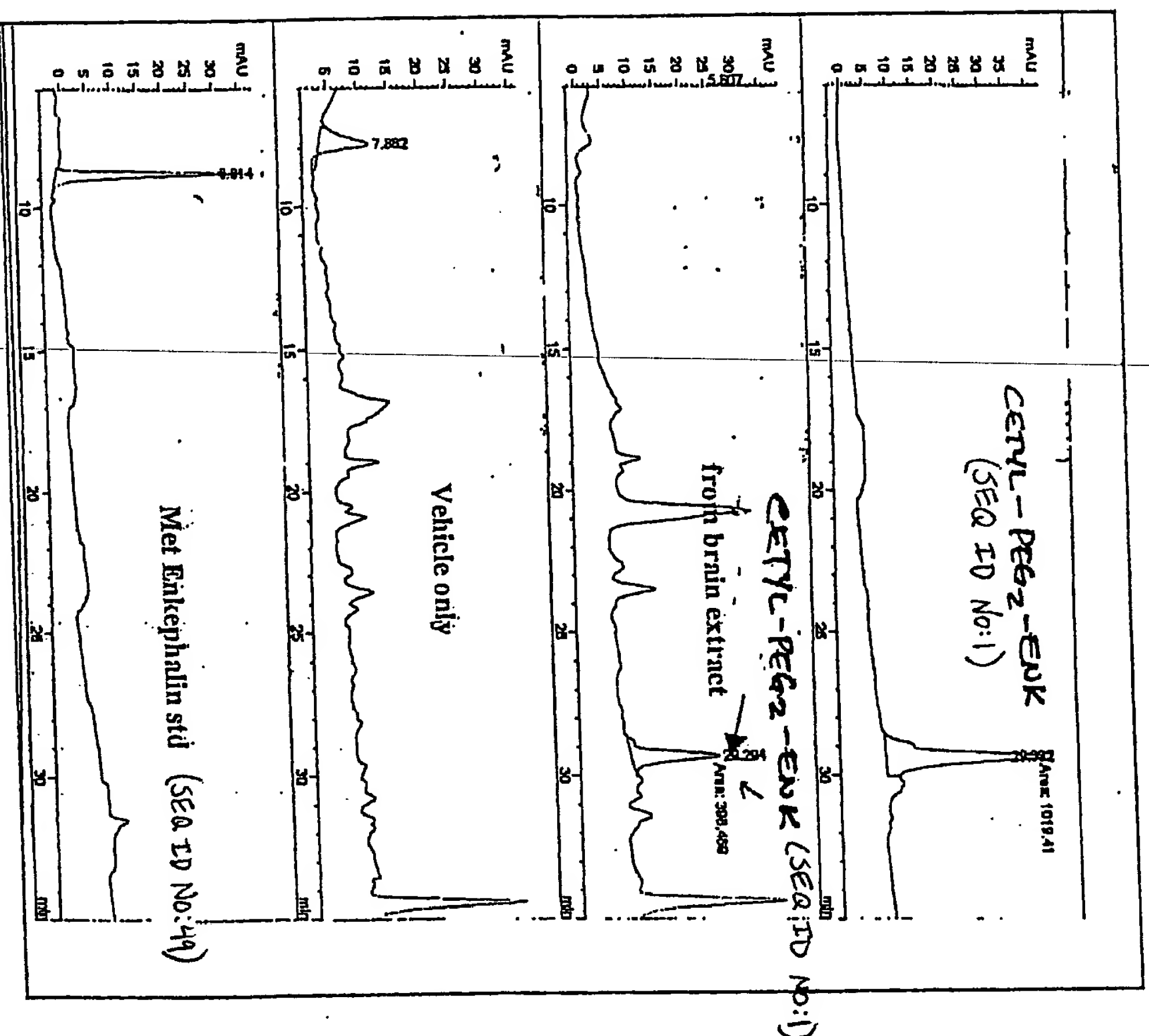
(SEQ ID No:1) Isolation of Cetyl-PEG₂-Enkephalin from the Brain

FIGURE 5A

FIGURE 5B

FIGURE 5C

FIGURE 5D



HPLC conditions:
 Column: C-18
 Solvent: solvent A: IPA
 solvent B: Water
 +0.1% TFA
 Gradient: linear

Naloxone Antagonism of Cetyl-PEG₂-Enkephalin-Induced Analgesia

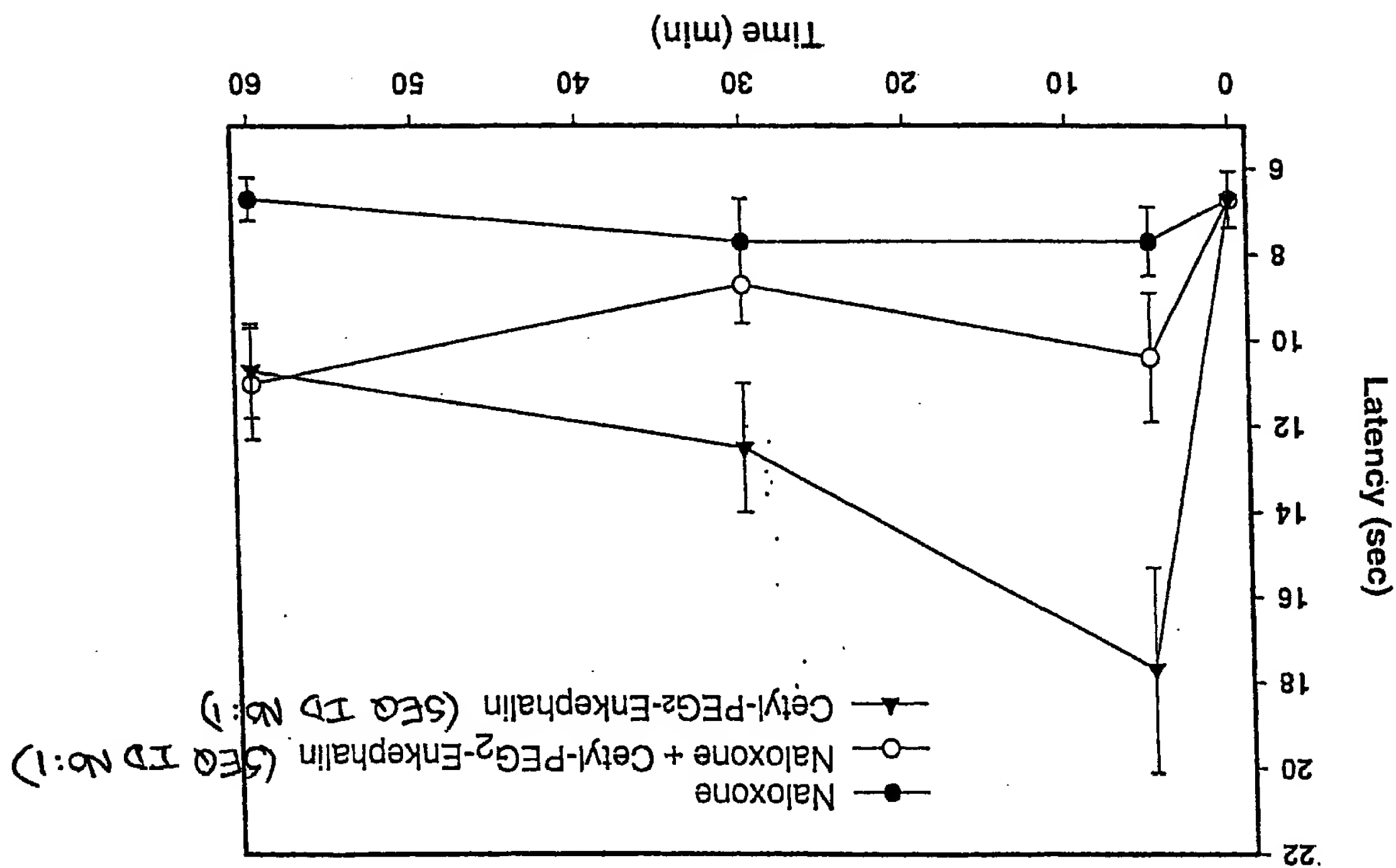


FIGURE 6

Analgesic Effect of a 5 mg/kg IV Dose of Cetyl-PEG₂-Enkephalin (SEA ID No:1) Monoconjugate in the Rat Hot-Plate Assay

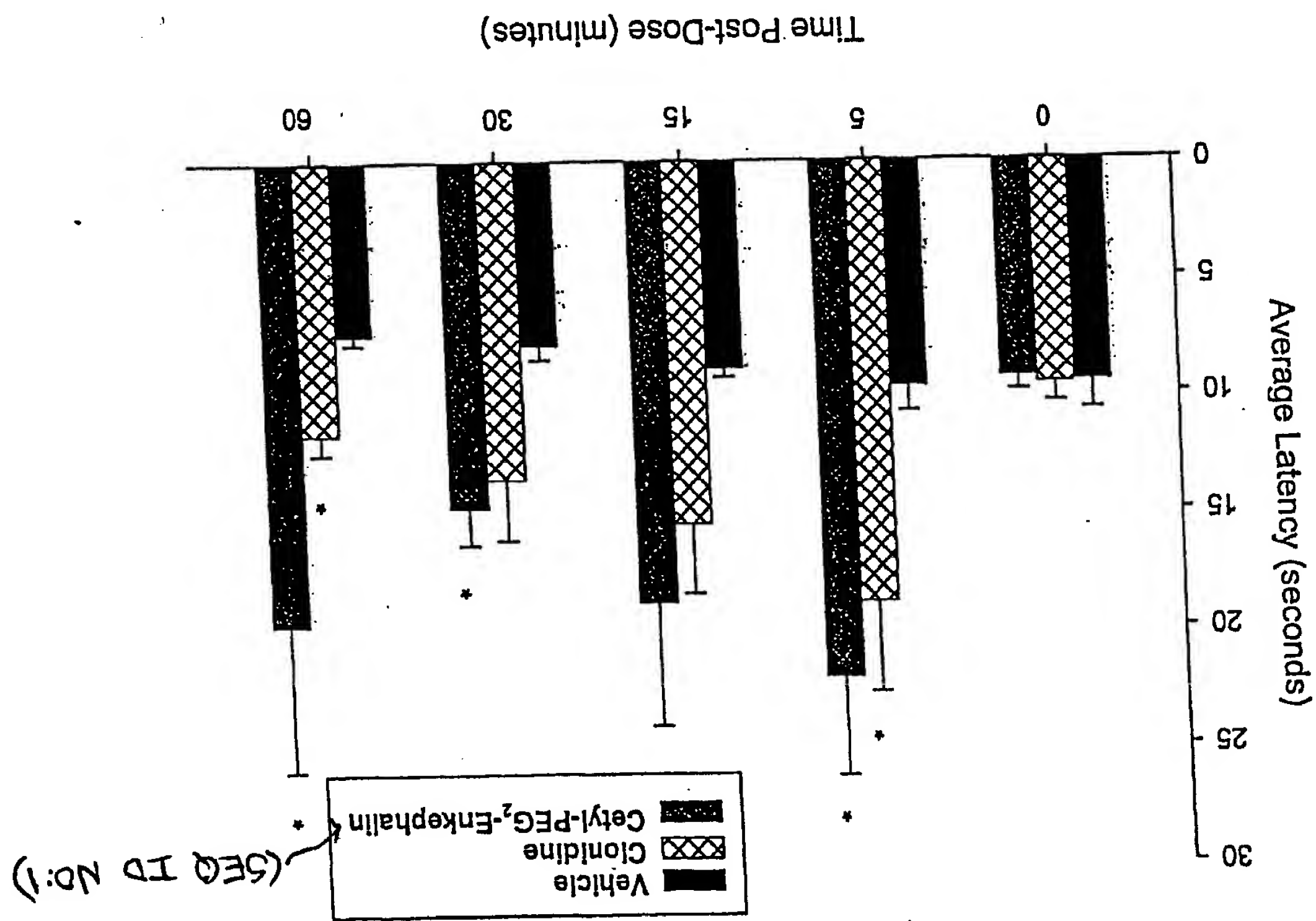


FIGURE 1

COMPARISON OF μ -RECEPTOR BINDING AFFINITY OF ENKEPHALIN CONJUGATES		
DRUG OR CONJUGATE	DETAILED STRUCTURE	% SPECIFIC BINDING*
Naloxone	Naloxone	100
Enkephalin	Met-Enkephalin -Lys (5EQ ID No:49)	67
Cetyl-ENK	Cetyl-PEG ₂ -ENK (5EQ ID No:1)	100
Chol-ENK	Cholesterol-PEG ₃ -ENK (5EQ ID No:1)	95
DHA-ENK	DHA-PEG ₂ -ENK (5EQ ID No:1)	63
Palm-ENK	Palmitate-PEG ₃ -ENK (5EQ ID No:1)	76
Cetyl-TEG-ENK	Cetyl-PEG ₃ -ENK (5EQ ID No:1)	100

*Data are based on percent inhibition at a concentration of 100nM. The radioligand was DAMGO ([D-Ala²,N-Me-Phe-Gly⁵-ol]enkephalin) and naloxone served as the reference.

FIGURE 8